REMARKS

Reconsideration is requested.

Claims 11-51 have been canceled, without prejudice. Claims 1-10 will be pending upon entry of the present Amendment. Entry of the Amendment and rejoinder and allowance of claim 10 with claims 1-9 are requested.

The claims have been revised, without prejudice, to advance prosecution. Support for the amendments may be found throughout the specification, such as at page 4, lines 21-25. No new matter has been added. The amendments to not raise new issues requiring further search and/or consideration. Entry of the present Amendment is requested.

The Examiner has found the applicants Rule 131 Declaration filed June 8, 2009 to allegedly be "unpersuasive" to antedate the Examiner's primary reference (i.e., Hauf (Journal of Cell Biology, Vol. 161, No, 2, April 28, 2003, pp 281-294)). Specifically, the Examiner asserts that the evidence relied upon in the Declaration (i.e., Anand et al. "AURORA-A amplification overrides the mitotic spindle assembly checkpoint, inducing resistance to Taxol" Cancer Cell, January 2003, volume 3, pp 51-62):

> "does not provide sufficient teaching for the invention as currently claimed. Applicant is currently claiming a combination of taxol and Aurora kinase inhibitor, which is taught by Hauf et al, whereas Anand et al, while being directed to the mitotic spindle assembly inhibitor paclitaxel, does not teach the use of Aurora kinase inhibitors. Anand et al rather addresses the negative effects associated with Aurura-A over-expression by utilizing *BUB1* which affects the spindle checkpoint which the Aurura-A is having a negative effect upon, rather than inhibiting Aurura kinase. Therefore, Applicant's arguments are not found persuasive since Anand et al is not teaching the same invention/combination as

> either Hauf et al or the instantly claimed invention." See pages 3-4 of the Office Action dated October 14, 2009.

The Examiner is requested to see however page 51 of Anand et al which describes the following (underlined emphasis added):

> "SIGNIFICANCE ... Our findings have important implications for cancer chemotherapy. They suggest that *AURORA-A* amplification will predict poor responsiveness to Taxol and other agents that target the spindle checkpoint. If so, inhibitors of Aurora-A activity may be a valuable adjunct to these agents in the treatment of cancers that overexpress *AURORA-A*."

One of ordinary skill in the art will appreciate from the above, and the whole of Anand et al, that the present inventors specifically state in Anand et al that inhibitors of Aurora-A activity may be used in combination with agents that target the spindle checkpoint for the treatment of cancers that overexpress AURORA-A. This is a clear and explicit disclosure of the subject matter of the claimed invention. Anand et al explicitly discloses the use of Aurora kinase inhibitors in combination with mitotic spindle assembly inhibitors and therefore teaches the invention of the instant claims.

The Examiner is believed to have previously appreciated that Anand et al teaches that the combination of Hauf would be useful in the claimed method. Specifically, the Examiner stated as follows on page 5 of the Office Action dated February 6, 2009 (underlined emphasis added):

> "Said combination of paclitaxel and heperadin would have an effect on breast cancer cells. This is evidenced by Anand teaching that paclitaxel functions to treat breast cancer by causing the cells to proceed to apoptosis (see page 59, first column, last paragraph), and Anand also teaches that AURORA-A over-expression is present in breast cancer (see page 51, "significance") and functions to disrupt the spindle

> checkpoint that is activated by paclitaxel (see page 59, first column, last paragraph, through second column, first paragraph). This reads on **instant claims 1-5 and 8-9**."

As noted in the above-quoted passage, the Examiner has more-recently asserted in the Office Action dated October 14, 2009 that

> "Anand et al ... does not teach the use of Aurora kinase inhibitors." See pages 3-4 of the Office Action dated October 14, 2009.

With due respect to the Examiner, the applicants submit that one of ordinary skill in the art will appreciate from Anand et al that the applicants were in possession of the claimed invention prior to the publication of Hauf. Hesperadin was a known Aurora A kinase inhibitor. See for example, page 6, lines 17-24 of the specification. Taxol (i.e., paclitaxel) was known to target the spindle checkpoint. See for example, page 2, line 12 through page 3, line 33 of the specification. Anand et al describes a new and useful combination in a method of treatment, as claimed.

The previously-filed Rule 131 Declaration is submitted to be persuasive in antedating the primary reference and reconsideration of same is respectfully requested.

The Section 103 rejection of claims 1-5, 8 and 9 over Hauf (Journal of Cell Biology, Vol. 161, No, 2, April 28, 2003, pp 281-294), is traversed. Reconsideration and withdrawal of the rejection are requested in view of the above, the previously-filed evidence and remarks, and the following distinguishing comments.

The Examiner has asserted in the Office Action of October 14, 2009 that Hauf discloses that:

> ...hesperadin can be used to allow cells treated with paclitaxel to stabilize at a faster rate based on the interaction with the spindle assembly checkpoint. ...
>
> The findings of Hauf indicate that hesperadin inhibits Aurora B and that Aurora B is required for spindle assembly in human cells.

The Examiner concludes that Hauf teaches that the combination of paclitaxel and heperadin would have an effect on breast cancer cells.

The results of the experiments of Hauf teach, as described by Hauf at page 288, left column, that

> "The spindle checkpoint is also activated by taxol (paclitaxel), which stabilizes microtubules. Surprisingly, when cells arrested with taxol were treated with Hesperadin, they exited mitosis within 1 h."

In other words, Hauf teaches that hesperadin overrides the spindle assembly checkpoint in taxol treated cells, thereby negating the apoptotic effect of taxol.

This is shown In Figure 8 of Hauf, which demonstrates that paclitaxel induces mitotic arrest by triggering the spindle assembly checkpoint, whereas hesperadin over-rides the spindle assembly checkpoint, thereby opposing the effects of paclitaxel. These findings therefore would imply to one of ordinary skill in the art that the two drugs in combination will antagonise one another.

The experiments of Hauf therefore suggest that hesperadin has an antagonistic effect on paclitaxel and hesperadin acts to inhibit the apoptotic effect of paclitaxel. Hauf therefore teaches that the effect of paclitaxel is reduced by the addition of hesperadin. The claimed invention would not have been obvious from the teachings of Hauf as to have combined paclitaxel and hesperadin to treat cancer would have been contrary to

Hauf. Hauf suggests that combination of taxol with hesperadin, would lead to reduction in the anti-cancer effects of taxol.

Furthermore, the teaching of Hauf relates to Aurora-B kinase and its inhibition by hesperadin. By contrast, the instant claims relate to the inhibition of Aurora-A kinase. Aurora-A kinase is not suggested by the Aurora-B kinase described in Hauf.

The applicants have sufficiently antedated Hauf. Moreover, Hauf fails to teach or suggest the claimed invention.

Withdrawal of the Section 103 rejection of claims 1-5, 8 and 9 over Hauf is requested.

The Section 103 rejection of claim 6 over Hauf in view of Slamon (New England Journal of Medicine, Vol. 344, No. 11, pages 783-792) "as evidenced by" Lange (EMBO Journal, Vol. 21, No. 20, pp 5364-5374), is traversed. Reconsideration and withdrawal of the rejection are requested for reasons noted above with regard to the patentability of claim 1 over Hauf as claim 6 depends from and includes the details of claim 1 and the further teachings of the Examiner's secondary references fail to cure the deficiencies of Hauf.

The Section 103 rejection of claim 7 over Hauf in view of Obermiller (Breast Cancer Research 2000, 2:28-31) "as evidenced by" Lange is traversed. Reconsideration and withdrawal of the rejection are requested for reasons noted above with regard to the patentability of claim 1 over Hauf as claim 7 depends from and includes the details of claim 1 and the further teachings of the Examiner's secondary references fail to cure the deficiencies of Hauf.

The claims are submitted to be in condition for allowance. Entry of the present Amendment and a Notice of Allowance are requested. The Examiner is requested to contact the undersigned, preferably by telephone, in the event anything further is required.

Respectfully submitted,

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